

What is claimed is:

1. A method of detecting one or more complexes of proteins, the method comprising the
5 steps of:

providing for each of the one or more complexes a cleaving probe specific for a first
protein in each of the one or more complexes, each cleaving probe having a cleavage-inducing
moiety with an effective proximity;

10 providing one or more binding compounds specific for a second protein of each of the
one or more complexes, such that each binding compound has one or more molecular tags each
attached thereto by a cleavable linkage, and such that the one or more molecular tags attached to
different binding compounds have different separation characteristics so that upon separation
molecular tags from different binding compounds form distinct peaks in a separation profile;

15 mixing the cleaving probes, the binding compounds, and the one or more complexes
such that cleaving probes specifically bind to first proteins of the complexes and binding
compounds specifically bind to the second proteins of the complexes and such that cleavable
linkages of the binding compounds are within the effective proximity of cleavage-inducing
moieties of the cleaving probes so that molecular tags are released; and

20 separating and identifying the released molecular tags to determine the presence or
absence or the amount of the one or more complexes of proteins.

2. The method of claim 1 wherein said step of mixing includes generating an active species
by said cleavage-inducing moiety, the active species cleaving said cleavable linkages with said
effective proximity.

25 3. The method of claim 2 wherein said cleavage-inducing moiety is a photosensitizer and
said active species is singlet oxygen.

4. The method of claim 2 wherein said separation characteristic is electrophoretic mobility
30 and wherein said separation profile is an electropherogram.

5. The method according to claims 1, 2, 3, or 4 wherein said one or more complexes of
proteins comprise up to three complexes, and wherein said one or more binding compounds
comprise up to three binding compounds.

6. The method of claim 5 wherein each of said cleaving probes and said one or more binding compounds comprises an antibody binding composition.

7. The method of claim 6 wherein said one or more complexes includes a complex comprising a Her3 receptor and a PI3 kinase.

8. The method of claim 7 wherein said Her3 receptor is said first protein whenever said PI3 kinase is said second protein, and wherein said PI3 kinase is said first protein whenever said Her3 receptor is said second protein.

9. The method of claim 6 wherein said one or more complexes include a complex comprising said first protein and said one or more second proteins each selected from the group consisting of a receptor tyrosine kinase, Grb2, SOS, Ras, and Raf, with the proviso that said first protein is different from said one or more second proteins.

10. The method of claim 9 wherein said receptor tyrosine kinase is a human receptor tyrosine kinase selected from the group consisting of Her1, Her2, Her3, Her4, IGF-1R, VEGFR1, VEGFR2, PDGFR α , and PDGFR β .

11. A method of detecting in a biological sample a complex comprising a first protein and one or more second proteins, the method comprising the steps of:

providing a cleaving probe specific for an antigenic determinant of the first protein, the cleaving probe having a cleavage-inducing moiety with an effective proximity;

providing one or more binding compounds each specific for an antigenic determinant of a second protein, such that each binding compound has one or more molecular tags each attached thereto by a cleavable linkage, and such that the one or more molecular tags attached to different binding compounds have different separation characteristics so that upon separation molecular tags from different binding compounds form distinct peaks in a separation profile;

mixing the cleaving probe, the one or more binding compounds, and the biological sample such that the cleaving probe specifically binds to the first protein and the one or more binding compounds specifically bind to the one or more second proteins, and such that cleavable linkages of the binding compounds are within the effective proximity of cleavage-inducing moieties of the cleaving probes so that molecular tags are released; and

separating and identifying the released molecular tags to determine the presence or absence or the amount of the complex in the biological sample.

12. The method of claim 11 wherein at least one of said second proteins is different than said first protein.

5 13. The method of claim 12 wherein said step of mixing includes generating an active species by said cleavage-inducing moiety, the active species cleaving said cleavable linkages with said effective proximity.

10 14. The method of claim 13 wherein said cleavage-inducing moiety is a photosensitizer and said active species is singlet oxygen.

15. The method of claim 13 wherein said separation characteristic is electrophoretic mobility and wherein said separation profile is an electropherogram.

15 16. The method according to claims 11, 12, 13, 14 or 15 wherein cleaving probe and said one or more binding compounds comprises an antibody binding composition.

17. The method of claim 16 wherein said complex comprises a Her3 receptor and a PI3 kinase.

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18. The method of claim 17 wherein said Her3 receptor is said first protein whenever said PI3 kinase is said second protein, and wherein said PI3 kinase is said first protein whenever said Her3 receptor is said second protein.

25 19. The method of claim 16 wherein said complex comprises said first protein and said one or more second proteins each selected from the group consisting of a receptor tyrosine kinase, a Shc protein, a Grb2 protein, an SOS protein, a Ras protein, and a Raf protein, with the proviso that said first protein is different from said one or more second proteins.

30 20. The method of claim 19 wherein said receptor tyrosine kinase is a human receptor tyrosine kinase selected from the group consisting of Her1, Her2, Her3, Her4, IGF-1R, VEGFR1, VEGFR2, PDGFR α , and PDGFR β .

35 21. A method of detecting in a biological sample a complex comprising a first protein and one or more second proteins, the method comprising the steps of:

providing one or more binding compounds each specific for a different antigenic determinant of the first protein, and providing one or more binding compounds each specific for a different antigenic determinant of a second protein, such that each binding compound has one or more molecular tags each attached thereto by a cleavable linkage, and such that the one or more molecular tags attached to different binding compounds have different separation characteristics so that upon separation molecular tags from different binding compounds form distinct peaks in a separation profile, and such that at least one of the second proteins is different from the first protein;

combining the biological sample and the one or more binding compounds specific for the first protein and for the one or more second proteins of the complex such that the binding compounds specifically bind to their respective antigenic determinants whenever such antigenic determinants are available and are unbound whenever such antigenic determinants are unavailable;

cleaving the cleavable linkages of the one or more binding compounds specifically bound to the complex so that molecular tags are released; and

separating and identifying the released molecular tags to determine the presence or absence or the amount of the complex in the biological sample.

22. The method of claim 21 further including, prior to said step of cleaving, a step of separating said unbound binding compounds from said binding compounds specifically bound to said complex.

23. The method of claim 22 wherein said separation characteristic is electrophoretic mobility and wherein said separation profile is an electropherogram.

24. The method according to claims 21, 22, or 23 wherein each of said one or more binding compounds comprises an antibody binding composition.

25. The method of claim 24 wherein said complex comprises a Her3 receptor and a PI3 kinase.

26. The method of claim 25 wherein said Her3 receptor is said first protein whenever said PI3 kinase is said second protein, and wherein said PI3 kinase is said first protein whenever said Her3 receptor is said second protein.

27. The method of claim 24 wherein said complex comprises said first protein and said one or more second proteins each selected from the group consisting of a receptor tyrosine kinase, a Shc protein, a Grb2 protein, an SOS protein, a Ras protein, and a Raf protein, with the proviso that said first protein is different from said one or more second proteins.

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28. The method of claim 27 wherein said receptor tyrosine kinase is a human receptor tyrosine kinase selected from the group consisting of Her1, Her2, Her3, Her4, IGF-1R, VEGFR1, VEGFR2, PDGFR α , and PDGFR β .

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